

REMARKS

Claims 1, 3, 4, 10, and 12 are pending in the present application.

I. REJECTIONS UNDER 35 U.S.C. §101/112 FOR LACK OF UTILITY

The Examiner rejected claims 1, 3, 4, 10, and 12 under 35 U.S.C. § 101 for a lack of patentable utility due to a lack of either specific and/or substantial utility or a well established utility.

The Examiner contends on page 3 of the Office Action that neither the specification nor the response disclose any associated phenotypes for the claimed polynucleotides. The Examiner further contends on page 4 of the Office Action that the specification does not disclose what the functions of the claimed polynucleotides are. Applicants submit that lacking assertion of utility does not mean the invention has no utility. According to MPEP 2107, if the applicant has not asserted any specific and substantial utility for the claimed invention, rejections under 35 U.S.C. § 101 and 112 shift the burden of coming forward with evidence to the applicant to: (i) explicitly identify a specific and substantial utility for the claimed invention; and (ii) provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. Specific and substantial utility for the claimed invention and evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing are presented in the present response.

The Examiner contends on page 3 of the Office Action that the method of isolation of the polynucleotides and oligonucleotides do nothing to the physical structure of the products and therefore, the method of their isolation is irrelevant to the patentability of the products. Applicants submit that due to the method of isolation of the present polynucleotides and oligonucleotides, the claimed polynucleotides and oligonucleotides are preselected and do not belong to the broad class of genomic DNA fragments. When a polynucleotide or oligonucleotide does not do a certain thing that is done in many genes within the genome, it takes the polynucleotide or oligonucleotide out of the broad class of random DNA in the genome. Accordingly, the claimed polynucleotides and oligonucleotides do not belong to the broad class of random DNA in the genome but belong to a subset within the broad class of genes. Thus, the polynucleotides and oligonucleotides do *not* have a general utility, but a specific utility.

As discussed in the Amendment filed on April 7, 2003, Applicants submit that the gene trap method enriches for a class of genes that are not required for teratocarcinoma cell viability and are likely to be involved in late stages of cellular differentiation and development.

Applicants submit that according to the Guidelines for the Utility Requirement (“Utility Guidelines”), 66 FR 1098 Jan. 5, 2001; MPEP 2107.01, a claim to a polynucleotide whose use is disclosed simply as a “gene probe” or “chromosome marker” would not be considered to be specific in the absence of a disclosure of a specific DNA target. According to the Utility Guidelines, a “specific utility” is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. The Utility Guidelines indicate that since any gene can be used as a “gene probe” or “chromosome marker”, there is a lack of specific utility if there is no specific DNA target. Accordingly, any gene or fragment of DNA sequence that is present in the human genome would fall within this broad class of the invention. However, the claimed polynucleotides of the present invention can be used as a gene probe or chromosome marker *specific* for such genes that are of particular interest to scientists and medical practitioners studying the biology of cellular differentiation and development. While the asserted utility is not as narrowly defined as that of a correlation with a disease condition, and although the number of polynucleotides that have such a specific utility is relatively larger than that of polynucleotides associated with a Mendelian genetic disease, Applicants submit that, it is nevertheless *not* a general utility that would be applicable to the broad class of genes in the genome. As such, Applicants submits that the claimed invention meets the threshold requirement of having specific utility.

Since the Applicants have asserted specific and substantial utility for the claimed invention, *inter alia*, on page 12, lines 8 to 24 of the specification, the Examiner is required to establish a *prima facie* case for lack of specific and substantial utility. The Guidelines for the Utility Requirement provides that where the asserted utility appears not to be specific or substantial, a *prima facie* showing must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The *prima facie* showing must contain the following elements (see MPEP 2107(II)(C)(1) and 2107.02(IV)) : (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established; (2) support for factual findings relied upon in reaching this conclusion; and (3) an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. The Examiner has not provided any factual findings in which the conclusion for lack of specific and substantial utility is relied upon, nor has the Examiner evaluated utilities taught in the closest prior art. Accordingly, the Examiner has not provided a *prima facie* showing that the invention does not have specific and substantial utility. The rejection is thus in error and should be withdrawn.

The Examiner contends on page 5 of the Office Action that Applicants' statement regarding usefulness of the claimed polynucleotides and oligonucleotides, at best, is guessing at substantial utility. However, Applicants submit that according to MPEP 2107.02(VII), evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. The character and amount of evidence needed to support an asserted utility will vary depending on whether the asserted utility appears to contravene established scientific principles and beliefs. *In re Gazave*, 379 F.2d 973, 978, 154 USPQ 92, 96 (CCPA 1967); *In re Chilowsky*, 229 F.2d 457, 462, 108 USPQ 321, 325 (CCPA 1956). Applicants have provided support derived through scientific logic to show that the gene trap method enriches a class of genes that is involved in late stages of stem cell differentiation and development as discussed in the remarks filed April 7, 2003. Accordingly, Applicants have provided sufficient evidence, to meet the threshold requirement that the asserted utility is more likely than not true.

The Examiner contends on page 5 of the Office Action that the usefulness of a claimed compound in terms of possible use is so general as to be meaningless. According to applicable case law, applicants do not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt" or in this case "definitely ascertained". *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965). Nor must an applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty. *Nelson v. Bowler*, 626 F.2d 853, 856-57, 206 USPQ 881, 883-84 (CCPA 1980). The Examiner is apparently questioning the credibility of the statement and not the credibility of utility. However, it is unclear what is the Examiner's basis for disbelieving Applicants' assertion. Applicants submit that, at least in regard to the requirements to show pharmacological activities for a compound, a 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' suffices. *Fujikawa v. Wattanasin*, 93 F.3d 1559; 39 USPQ2d 1897 (Fed. Cir. 1996). In fact, all that is required in evaluating the credibility of an asserted utility is a preponderance of the totality of the evidence under consideration. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). A preponderance of the evidence exists when it suggests that it is more likely than not that the assertion in question is true. *Herman v. Huddleston*, 459 U.S. 375, 390 (1983). Still further, according to the Guideline, office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement. Accordingly, the assertion that the genes identified in the present invention are likely involved in

the late stages of stem cell differentiation and development absent any countervailing evidence, satisfies the threshold of the utility requirement.

The Examiner contends on page 6 of the Office Action that the instant application discloses no such information other than general statements which could be true or false, verifiable only after conducting further research on the claimed polynucleotides and oligonucleotides. In the present application, the utility of the claimed invention would be immediately appreciated by those familiar with the technological field of the invention such as biologists studying cellular differentiation and development. Applicants submit in the amendment filed April 7, 2003 that, among other uses, the polynucleotides of the present invention may be used as a research tool in the context of a hybridization assay, e.g., in the format of a microarray. Instead of using the entire universe of genes in the genome in such an experiment, the skilled person has the option of limiting the experiment to using polynucleotides of the invention in the microarray. In effect, genes that are critically essential to the survival and early growth of teratocarcinoma cells would be excluded from the microarray. The use of polynucleotides of the present invention help cut down the total number of genes that needs to be studied and simplify the work of a biologist who uses this research tool to study embryonic cell differentiation and development. Thus, no further research is required to identify or reasonably confirm the asserted utility. Applicants submit that the guidelines cautioned not to interpret “immediate benefit to the public” to mean that products or services based on the claimed invention must be “currently available” to the public in order to satisfy the utility requirement. *Brenner v. Manson*, 383 U.S., 519, 534-35, 148 USPQ 689, 695 (1966). Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a “substantial” utility. Here, the set of genes that are enriched for their lack of involvement in cell viability and their likelihood of participating in the late stages of embryonic cell differentiation and their development represents substantial utility to biologists who are studying late stages of cellular differentiation and development. The preselected set of genes are currently available and will immediately provide, at a minimum, the economic benefit of not having to put every gene in the genome on microarray(s). Accordingly, the present invention has substantial utility.

For the claimed utility to be credible, the invention must be “believable based on the record or the nature of the invention” M.P.E.P. 2107.02(III)(A). Applicants assert that because of the nature of the invention and for the reasons set forth above, the utility of the claimed polynucleotides are specific, substantial and credible. Applicants respectfully request that rejection under 35 U.S.C. § 101 be withdrawn.

Claims 1, 3, 4, 10, and 12 are also rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility. Applicants submit that when an Applicant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn. Thus, Applicants respectfully request that the rejection of claims 1, 3, 4, 10, and 12 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Examiner alleges on page 7 of the Office Action that the specification fails to disclose a specific and substantial utility for the claimed invention in the capacity of detecting polymorphisms, because it does not disclose whether the claimed nucleic acid molecules can, in fact, be used to detect any polymorphism whatsoever. Applicants submit that it is not necessary that the claimed polynucleotides detect a polymorphism or diagnose or detect a disease or disorder. As indicated in MPEP 2164.01(c), when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection based on how to use. If any use of the claimed invention is enabled when multiple uses are disclosed, the application is enabling for the claimed invention. Since the specification teaches at least one enabling use, the enablement requirement is satisfied. Applicants respectfully request that the rejection of claims 1, 3, 4, 10 and 12 under 35 U.S.C. §§ 101 and 112, first paragraph, be withdrawn.

II. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH FOR LACK OF WRITTEN DESCRIPTION

Claims 1, 3, 4, 10, and 12 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner alleges on page 9 that the disclosed subgenus and species embraced by the claims are not representative of the entire genus being claimed and that the specification does not disclose encoding sequences or open reading frames (ORFs). This is contrary to the requirement under case law that “Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *Vas-Cath Inc. v. Mahurka* 1935 F.2d 1555, 19USPQ2d 1111 (Fed. Cir. 1991). Furthermore, case law also supports the fact that for chemical material, when one skilled in the art can distinguish a formula from others and can identify many of the species that the claims encompass, there is adequate description of the claimed genus. *Hybritech v. Monoclonal Antibodies*, 802 F.2d 1367, 1384, 231 USPQ 81, 94; *Fonar Corp. v. General Electric Co.*, 107 F.3d 1543, 1549, 41 USPQ2d 1801, 1805. In the present case, Claim 3 recites nucleotides that comprise a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS: 9,

10, 12, 13, 14, and 16-18. As the exact structure of SEQ ID NOS: 9, 10, 12, 13, 14, and 16-18 are provided in the specification, although there are numerous polynucleotides that falls within this description, a person of skill in the art can readily recognizes the polynucleotide as described in claim 3. As such, Applicants submit that adequate written description has been provided for Claims 1, 3, 4, 10, and 12.



CONCLUSION

Applicants submit that Claims 1, 3, 4, 10, and 12 satisfy all of the criteria for patentability and are in condition for allowance. Accordingly, Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application.

Respectfully submitted,

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